What is claimed is:

1. An nucleic acid molecule encoding an altered CTSC protein, said nucleic acid having at least one of the alterations set forth in Table 1.

2. A nucleic acid probe specifically hybridizable to a human altered CTSC-encoding nucleic acid and not to wild-type CTSC encoding nucleic acids, said altered CTSC encoding nucleic acid having one of the alterations set forth in Table 1.

3. The nucleic acid probe of claim 2 wherein said altered CTSC DNA has the alteration comprising a substitution of a C for a T at nucleotide position 856 in Exon 6, thereby replacing a codon encoding glutamine for a stop codon.

4. The nucleic acid probe of claim 2 wherein said altered CTSC DNA has the alteration comprising a substitution of an A for a G at nucleotide position 857 in Exon 6, thereby replacing a codon encoding glutamine for an arginine encoding codon.

5. The nucleic acid probe of claim 2 wherein said altered CTSC DNA has the alteration comprising a deletion of an A at nucleotide position 1047 in Exon 7, thereby causing a frameshift and a premature stop codon.

6. The nucleic acid probe of claim 2 wherein said altered CTSC DNA has the alteration comprising a deletion of a dinucleotide CT at nucleotide positions 1028 and 1029 in Exon 7, thereby causing a premature stop codon.

7. The nucleic acid probe of claim 2 wherein said altered CTSC DNA has the alteration comprising a

substitution of a G for a A at nucleotide position 1286 in Exon 7, thereby replacing a tryptophan codon with a premature stop codon.

8. The nucleic acid probe of claim 2 wherein said altered CTSC DNA has the alteration comprising a substitution of a C for a T at nucleotide position 1015 in Exon 7, thereby replacing a codon encoding arginine for a cysteine encoding codon.

9. The nucleic acid probe of claim 2 wherein said altered CTSC DNA has the alteration comprising a substitution of an A for a G at nucleotide position 1019 in Exon 7, thereby replacing a codon encoding tyrosine for a cysteine encoding codon.

10. The nucleic acid probe of claim 2 wherein said altered CTSC DNA has the alteration comprising a substitution of an A for a G at nucleotide position 1040 in Exon 7, thereby replacing a codon encoding tyrosine for a cysteine encoding codon.

11. A mutated CTSC protein encoded by a CTSC encoding nucleic acid, said nucleic acid containing a mutation as set forth in Table 1.

12. An antibody immunologically specific for the protein of claim 11.

13. A method for detecting a germline alteration in a CTSC gene, said alteration selected from the group consisting of the alterations set forth in Table 1 in a human, said method comprising analyzing a sequence of a CTSC gene or CTSC RNA from a human sample or analyzing a sequence of CTSC cDNA made from mRNA from said human sample.

14. The method of claim 13 which comprises

analyzing CTSC RNA from the subject.

15. The method of claim 14 wherein a germline alteration is detected by hybridizing a CTSC gene probe which specifically hybridizes to nucleic acids containing at least one of said alterations and not to wild-type CTSC sequences to RNA isolated from said human sample and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said alteration in said RNA and thereby the presence of said germline alteration in said sample.

16. The method of claim 13 wherein a germline alteration is detected by obtaining a first CTSC gene fragment from a CTSC gene isolated from said human sample and a second CTSC gene fragment from a wild-type CTSC gene, said second fragment corresponding to said first fragment, forming single-stranded DNA from said first CTSC gene fragment and from said second CTSC gene fragment, electrophoresing said single-stranded DNAs on a non-denaturing polyacrylamide gel, comparing the mobility of said single-stranded DNAs on said gel to determine if said single-stranded DNA from said first CTSC gene fragment is shifted relative to said second CTSC gene fragment and sequencing said single-stranded DNA from said first CTSC gene fragment having a shift in mobility.

17. The method of claim 13 wherein a germline alteration is detected by hybridizing a CTSC probe which specifically hybridizes to nucleic acids containing at least one of said alterations and not to wild-type CTSC sequences to genomic DNA isolated from said sample and detecting the presence of a hybridization product, wherein a presence of said product indicates the presence of said germline alteration in the sample.

18. The method of claim 13 wherein a germline

alteration is detected by amplifying all or part of a CTSC gene in said sample using a set of primers specific for a wild-type CTSC gene to produce amplified CTSC nucleic acids and sequencing the amplified CTSC nucleic acids.

19. The method of claim 13 wherein a germline alteration is detected by amplifying all or part of a CTSC gene in said sample using a primer specific for an allele having for one of said alterations and detecting the presence of an amplified product, wherein the presence of said product indicates the presence of said allele in the sample.

20. The method of claim 13 wherein a germline alteration is detected by molecularly cloning all or part of a CTSC gene in said sample to produce a cloned nucleic acid and sequencing the cloned nucleic acid.

21. The method of claim 13 wherein a germline alteration is detected by forming a heteroduplex consisting of a first strand of nucleic acid selected from the group consisting of CTSC gene genomic DNA fragment isolated from said sample, CTSC RNA fragment isolated from said sample and CTSC cDNA fragment made from mRNA from said sample and a second strand of a nucleic acid consisting of a corresponding human wild-type CTSC gene fragment, analyzing for the presence of a mismatch in said heteroduplex, and sequencing said first strand of nucleic acid having a mismatch.

22. The method of claim 13 wherein a germline alteration is detected by amplifying CTSC gene nucleic acids in said sample, hybridizing the amplified nucleic acids to a CTSC DNA probe which specifically hybridizes to nucleic acids containing at least one of said alterations and not to wild-type CTSC sequences and detecting the presence of a hybridization product,

wherein a presence of said product indicates the presence of said germline alteration.

23. The method of claim 13 wherein a germline alteration is detected by analyzing the sequence of a CTSC gene in said sample for one of the mutations set forth in Table 1.

24. The method of claim 13 wherein a germline alteration is detected by obtaining a first CTSC gene fragment from a CTSC gene isolated from said human sample and a second CTSC gene fragment from a CTSC allele specific for one of said alterations, said second fragment corresponding to said first fragment, forming single-stranded DNA from said first CTSC gene fragment and from said second CTSC gene fragment, electrophoresing said single-stranded DNAs on a non-denaturing polyacrylamide gel and comparing the mobility of said single-stranded DNAs on said gel to determine if said single-stranded DNA from said first CTSC gene fragment is shifted relative to said second CTSC gene fragment, wherein no shift in electrophoretic mobility indicates the presence of said alteration in said sample.

26. The method of claim 13 wherein a germline alteration is detected by obtaining a first CTSC gene fragment from (a) CTSC gene genomic DNA isolated from said sample, (b) CTSC RNA isolated from said sample or (c) CTSC cDNA made from mRNA isolated from said sample and a second CTSC gene fragment from a CTSC allele specific for one of said alterations, said second fragment corresponding to said first fragment, forming single-stranded DNA from said first CTSC gene fragment and from said second CTSC gene fragment, forming a heteroduplex consisting of single-stranded DNA from said first CTSC gene fragment and single-stranded DNA from

said second CTSC gene fragment and analyzing for the presence of a mismatch in said heteroduplex, wherein no mismatch indicates the presence of said alteration.

27. A method as claimed in claim 13, wherein said germline alteration comprises a substitution of a C for a T at nucleotide position 856 in Exon 6, thereby replacing a codon encoding glutamine for a stop codon.

28. A method as claimed in claim 13, wherein said germline alteration comprises a substitution of an A for a G at nucleotide position 857 in Exon 6, thereby replacing a codon encoding glutamine for an arginine encoding codon.

29. A method as claimed in claim 13, wherein said germline alteration comprises a deletion of an A at nucleotide position 1047 in Exon 7, thereby causing a frameshift and a premature stop codon.

30. A method as claimed in claim 13, wherein said germline alteration comprises a deletion of a dinucleotide CT at nucleotide positions 1028 and 1029 in Exon 7, thereby causing a premature stop codon.

31. A method as claimed in claim 13, wherein said germline alteration comprises a substitution of a G for a A at nucleotide position 1286 in Exon 7, thereby replacing a tryptophan codon with a premature stop codon.

32. A method as claimed in claim 13, wherein said germline alteration comprises a substitution of a C for a T at nucleotide position 1015 in Exon 7, thereby replacing a codon encoding arginine for a cysteine encoding codon.

33. A method as claimed in claim 13, wherein said germline alteration comprises a substitution of an A for a G at nucleotide position 1019 in Exon 7, thereby replacing a codon encoding tyrosine for a cysteine encoding codon.

34. A method as claimed in claim 13, wherein said germline alteration comprises a substitution of an A for a G at nucleotide position 1040 in Exon 7, thereby replacing a codon encoding tyrosine for a cysteine encoding codon.

35. A method for detecting a germline alteration in a CTSC human encoding nucleic acid, said method comprising comparing a sequence of a CTSC DNA or CTSC RNA from a human sample with an isolated wild type CTSC sequence as provided in SEQ ID NO:1.

36. A method as claimed in claim 35, wherein stability of said altered CTSC mRNA is compared with stability of wild type CTSC mRNA.

37. A method as claimed in claim 35, further comprising expressing an altered CTSC protein from said altered CTSC encoding nucleic acid and comparing cathepsin C enzymatic activity of said altered CTSC protein to enzymatic activity of wild-type cathepsin C.

38. A kit for detecting the presence of an altered CTSC encoding nucleic acid in a biological sample, comprising:

i) oligonucleotides which specifically hybridize with CTSC encoding nucleic acids having the alterations set forth in Table 1;

ii) reaction buffer; and

iii) an instruction sheet.

39. A kit as claimed in claim 38, wherein said oligonucleotide contains a tag.

40. A kit for detecting the presence an altered CTSC encoding nucleic acid in a biological sample, comprising:

i) antibodies immunologically specific for the altered CTSC proteins of the invention;

ii) a solid support with immobilized CTSC antigens as a positive control; and

iii) an instruction sheet.

41. A kit as claimed in claim 40, wherein said antibody contains a tag.